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AUTHOR REPLY

Male Infertility

Re: Sperm retrieval rates and intracytoplasmic sperm injection outcomes for men with non-obstructive azoospermia and the health of resulting offspring

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We are thankful to Dr. Drobnis for her insights and balanced comments with regard to our article titled "comparison of sperm retrieval and reproductive outcome in azoospermic men with testicular failure and obstructive azoospermia treated for infertility".[1]

Our main objective was to offer firm information that could be used as a counseling tool by doctors treating patients with azoospermia-related infertility. The key message was that non-obstructive azoospermia (NOA) negatively affect the success rates of both surgical sperm retrieval and live birth rates after intracytoplasmic sperm injection (ICSI), by approximately halving their results, but not the neonatal outcomes of the resulting offspring, when compared with obstructive azoospermia (OA). To achieve this conclusion, we compared sperm retrieval rates (SRR), ICSI outcomes and the neonatal profile of babies born in men with NOA and OA, after controlling for covariates that could potentially bias the results. We used microdissection testicular sperm extraction (micro-TESE) as a sperm acquisition method in our group of men with NOA to offer them the best possible chance of having sperm retrieved. For comparison, we included a subgroup of couples treated by ICSI with donor sperm due to failed micro-TESE. Interestingly, the magnitude of the aforementioned negative effects was also similar when NOA was compared with donor sperm, albeit not different between OA and donor sperm.

We agree with Dr. Drobnis that we could have added the outcomes in NOA according to the patients' testicular biopsy results and separately for men with Klinefelter syndrome (KS), owed to the limited information available in the literature for these subsets of patients. As far as KS is concerned, our dataset comprised eight men with KS, of whom four had sperm retrieved by micro-TESE and used for ICSI. Two pregnancies were obtained after ICSI using testicular sperm from KS patients, of which one resulted in a miscarriage at the 11-week gestation while the other in a delivery of health preterm twins at the 35 gestational week. We present SRR, ICSI outcomes and the profile of neonates born according to the patients' testicular biopsy results (**Table 1**). Patients with maturation arrest (MA) had lower SRR compared with those with sertoli-cell only (SCO) ($P = 0.007$). Both categories had lower SRR compared with hypospermatogeneis ($P < 0.001$). Live birth rates were lower in SCO compared with both hypospermatogenesis and MA after adjusting for covariates ($P = 0.01$), whereas the obstetrical outcomes of resulting offspring were not affected by the testicular histopathology categories. Our data indicate that SRR and live birth with ICSI are differentially affected by the severity of disruptive spermatogenesis in men with NOA. Nevertheless, the neonatal profile of resulting offspring was not affected by the severity of testicular failure.

Table 1: SRR, live birth and obstetrical outcome of resulted offspring according to testicular histology results in patients with non-obstructive azoospermia

	Hypospermatogenesis	*Maturation arrest*	*Sertoli cell-only*	*P*
Number of patients	84	67	205	-
Male age (year)	38.1±9.7	36.4±3.8	36.4±7.2	0.50
SRR[a] (*n*, %)	84 (100.0)	27 (40.3)	40 (19.5)	<0.001[b]
Live birth (*n*, %)	20 (23.8)	6 (22.2)	4 (10.0)	0.004[c]
Neonates born, (*n*)	31	11	6	-
Gestational age (week)	36.3±3.2	35.9±1.9	35.5±3.9	0.18
Birth weight (g)	2987±477	2629±870	2583±775	0.12

Data are means±SD unless otherwise indicated. Kruskal-Wallis; Pearson Chi-square test and Fisher exact test were used for comparisons. [a]Defined at obtaining sperm; [b]$P < 0.001$ when adjusting for male age and serum levels of FSH, LH and testosterone in a logistic regression model; [c]$P = 0.01$ when adjusting for covariates including female and male age, male endocrine profile, duration of infertility, associated female infertility factor and number of transferred embryos. SD: standard deviation; SRR: sperm retrieval rates; FSH: follicle stimulating hormone; LH: luteinizing hormone

Although our data indicate that the biopsy results have prognostic value for the chances of SR and live birth, we do not recommend routine testicular biopsy prior to sperm retrieval in men with NOA. An advanced site of sperm production can be found even in the worst case scenario of SCO.[2,3] Moreover, removal of testicular tissue with the sole purpose of histopathological evaluation could potentially remove foci of sperm production and thus jeopardize the chances of future successful retrieval attempts.[4] Our routine is to take a small testicular biopsy specimen during sperm retrieval for histologic confirmation of NOA.

COMPETING INTERESTS

The authors declare no competing interests.

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